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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/822,186	03/20/1997	DAVID C RUEGER	CRP-137	6062
7590	11/21/2001			
JAMES F. HALEY FISH & NEAVE 1251 AVENUE OF THE AMERICAS NEW YORK, NY 100201104			EXAMINER	
			ROMEON, DAVID S	
			ART UNIT	PAPER NUMBER
			1647	36
DATE MAILED: 11/21/2001				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	08/822,186	RUEGER ET AL.	
	Examiner	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) Responsive to communication(s) filed on 30 August 2001.

2a) This action is FINAL.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) Claim(s) 1-9,11-25,31-33,35 and 36 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-9,11-25,31-33,35 and 36 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) 1-9,11-25,31-33,35 and 36 are subject to restriction and/or election requirement.

**Application Papers**

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some \* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.	6) <input type="checkbox"/> Other: _____

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**DETAILED ACTION**

1. The amendment filed 08/30/2001 (Paper No. 35) has been entered. Claims 1-9, 11-33, 35 and 36 are pending. Claims 26-30 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention. Election was made **without** traverse in Paper No. 20. Applicant's elected without traverse OP-1, carboxymethyl cellulose, collagen, critical size defects in Paper No. 20. Claims 1-9, 11-25, 31-33, 35 and 36 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) to the extent that they are drawn to a non-elected species. Election was made **without** traverse in Paper No. 20. Claims 1-9, 11-25, 31-33, 35 and 36 are being examined to the extent that they read upon OP-1, carboxymethyl cellulose, collagen, critical size defects. Any objection and/or rejection of record that is not maintained and/or repeated in this Office action is withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 1, 7-9, 11-14, 20-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Amman (BA, cited by Applicants). Applicants argue that Amman does not specifically teach the combination of collagen and CMC. Applicants' arguments have been fully considered but they are not persuasive. Amman at page 10, lines 28-34, teaches that the polymer may be CMC or collagen or a combination of these. Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. Evidence of

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secondary considerations, such as synergism, is irrelevant to 35 U.S.C. 102 rejections and thus cannot overcome a rejection so based.

3. Claims 20, 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Beck (CA, cited by Applicants). Applicants argue that TGF- $\beta$  is not included as an osteogenic protein at page 22, lines 3-7. Applicants' arguments have been fully considered but they are not persuasive. There is no teaching in the specification that would exclude TGF- $\beta$  from being an osteogenic protein.

5 TGF- $\beta$  is an osteogenic protein as is manifestly obvious from the teachings of Beck.

4. Claims 1-5, 7-9, 11-13, 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Tucker (a33). Applicants' arguments have been fully considered but they are not persuasive. The 10 applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131. It is acknowledged that applicants will claim priority from this patent however, a 15 claim to priority does not appear to be germane because a showing that any invention disclosed

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but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," is necessary.

5. Claims 1-5, 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amman (BA, cited by Applicants) and Kuberampath (aa9). Applicants argue that Amman and  
Kuberampath, alone or in combination, do not teach or suggest the combined use of collagen and CMC with OP-1. Applicants' arguments have been fully considered but they are not  
persuasive. Amman at page 10, lines 28-34, teaches that the polymer may be CMC or collagen or a combination of these. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make an osteogenic device comprising TGF- $\beta$ 1, as taught by Amman,  
10 and to modify that teaching by making an osteogenic device comprising OP1, as taught by Kuberampath, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because Kuberampath teaches that OP1 is useful for the purposes for which Amman is intended, namely bone induction.

6. Claims 1, 6, 15, 16, 32, 33, 35, 36 are rejected under 35 U.S.C. 103(a) as being  
15 unpatentable over Amman (BA, cited by Applicants) and Ogawa (u4). Applicants' arguments have been fully considered but they are not persuasive. Amman at page 10, lines 28-34, teaches that the polymer may be CMC or collagen or a combination of these. Disclosed examples and

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preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. There is no teaching in the specification that would exclude TGF- $\beta$  from being an osteogenic protein. TGF- $\beta$  is an osteogenic protein as is manifestly obvious from the teachings of Amman. In response to applicant's arguments against the references individually, 5 one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references.

7. Claims 17-19, 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amman (BA, cited by Applicants) and Cook (CD, cited by Applicants) in view of Ogawa (u4). Applicants argue that Amman and Ogawa, alone or in combination, fails to teach the combined use of 10 collagen and CMC with OP-1 and that this deficiency is not remedied by Cook. Amman at page 10, lines 28-34, teaches that the polymer may be CMC or collagen or a combination of these. Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make an osteogenic device comprising TGF- $\beta$ 1, 15 collagen and CMC, as taught by Amman, and to modify that teaching by using 2.5 mg of OP1 per 500 mg of collagen, as taught by Cook, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because 2.5 mg of OP1 per 500 mg of collagen is useful for making osteogenic devices. It would have been obvious to one

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of ordinary skill in the art at the time of Applicants' invention to make an osteogenic device comprising OP1, collagen and CMC, as taught by Amman and Cook, and to modify that teaching by wetting the device with saline, as taught by Ogawa, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings in order to mold 5 the osteogenic device in to a shape suitable for implantation. The invention is *prima facie* obvious over the prior art.

### *Conclusion*

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. At page 12 of the preliminary amendment filed 12/07/2000 (Paper No. 32) Applicants 10 cite Handbook of Pharmaceutical Excipients, 2nd ed., A. Wade and P. J. Weller (eds), American Pharmaceutical Association, Washington, DC, January, 1994, page 80, paragraph 12, as evidence of unexpected results. See Exhibit 1 of Paper No. 32. However, the same reference also teaches that reports of incompatibilities or adverse reactions to an excipient, in a particular application, may not necessarily prevent its use in other situations (page xiii, column 1, full paragraph 1).
- 15 Weiss (a36) teaches that tropoelastin coacervates can be used to formulate slow release compositions of active ingredients or to form protective coatings for active ingredients using standard formulation techniques (column 9, lines 31-34).

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9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO 5 MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date 10 of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

15 IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

OFFICIAL PAPERS FILED BY FAX SHOULD BE DIRECTED TO (703) 308-4242.

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

20

*David Romeo*  
DAVID ROMEO  
PRIMARY EXAMINER  
ART UNIT 1647

NOVEMBER 19, 2001